16 Red Rowen Lane
Plymouth Meeting, PA 19462

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Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive
Room 1-23
Rockville, MD 20857

Subject: Docket No. 98D-0362
Site-Specific Stability Requirements for Drug and Biologic Applications

Dear Sir:

I attended the March 31, 1999 FDA Public meeting on Site-Specific Stability Data for Drug and Biologic Applications and I listened to the industry's objection to the site-specific stability requirements. I disagree with the PhRMA's position that site-specific stability is not necessary and that validation will assure that the stability will be satisfactory.

I agree with FDA's latest site-stability requirement based on the three tiered, risk-based system. It will assure that site changes involving drug substance and drug products manufactured at plant facilities and the proposed site of commercial manufacturing will not affect stability.

The following are my reasons based on more than 15 years of real world experience in process validation and equipment and facilities qualification for drug product both as a practitioner and as an auditor:

1. There are many products that failed process validation when its manufacture was transferred to a new site. I have seen serious stability failures caused by unknown factors even though the product has been validated.

2. There will always be seen and unseen changes during the transfer that will affect the stability. People training and expertise, product knowledge, equivalent manufacturing conditions, and use of equivalent equipment are some of the reasons for failure during the transfer. This is very true for old, grandfathered products that do not have historically robust product stability.

3. Not all validation protocols are alike. Acceptance criteria varies from long, detailed and strict to short, lacking and loose. In fact, due to the marketing push for the product, the process and specifications are still evolving and not yet fully optimized by the time the product is validated. Basically, you can tailor the validation so that you will pass the acceptance criteria.

Therefore, site-specific stability is needed for both drug substance and drug product.

Sincerely yours,

Luis S. Villacorta

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Luis S. Villacorta
16 Red Rowen Lane
Plymouth Meeting, PA USA 19462

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FOOD AND DRUG ADMINISTRATION
12420 PARKLAWN DRIVE
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ROCKVILLE, MD 20857